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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,558	05/25/2007	Nicolas Peter Shortis	17811US01	8274

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EXAMINER	
SPIVACK, PHYLLIS G	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,558	SHORTIS, NICOLAS PETER	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/24/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicants' Request for Continued Examination (RCE) filed June 24, 2009 under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), is acknowledged and accepted.

Claims 1-11 are pending, wherein the subject matter under consideration remains those methods of treating irritable bowel syndrome comprising administering balsalazide, or a salt thereof, as well as methods drawn to administering a 4-aminosalicylic acid compound or a 5-aminosalicyclic acid compound, either of which is modified to include a 4-aminobenzoyl-β-alanine side chain. Those methods drawn to the treatment of conditions other than irritable bowel syndrome remain withdrawn from consideration by the Examiner, 37 CFR 1.142(b), as drawn to non-elected inventions.

An Information Disclosure Statement filed June 24, 2009 is further acknowledged and has been reviewed.

Declarations filed under 37 CFR § 1.132 and under 37 CFR § 1.131, both on June 24, 2009, are further acknowledged and have been considered.

Those rejections set forth in prior Office Actions that are not herein reiterated are withdrawn. The following rejections are the only rejections presently applied to the instant claims.

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Parenthetical subject matter in claims 1 and 11, i.e., (and its complication diverticulitis), render the claims indefinite. It is unclear whether or not claim limitations are intended.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention.

The claims are directed to the prophylaxis of non-inflammatory irritable bowel syndrome or for the treatment of one or more of (a) non-inflammatory bowel disease, (b) diverticulosis (and its complication diverticulitis), (c) diarrhea-predominant irritable bowel syndrome, (d) irritable bowel syndrome, (e) one or more of bloating, diarrhea, cramping, pain, low abdominal pain, distension, wind, flatulence, gas production, fluid secretion, mucus production, constipation, urgency or incontinence, when associated with a non-inflammatory bowel disease, diarrhea-predominant irritable bowel syndrome or other non-specific non-inflammatory bowel disorder, f) non ulcer dyspepsia, (g) spastic colon, (h) unstable colonic neurosis, (i) spastic colitis, (j) mucous colitis, (k) alternating constipation/diarrhea, (l) alternating diarrhea and constipation type IBS or (m) constipation IBS, comprising administering to a patient in need of such treatment or prophylaxis an effective amount of balsalazide, or a salt thereof, or a composition comprising balsalazide, or a salt thereof, together with a suitable carrier.

The specification does not reasonably provide enablement for methods of prophylaxis or treatment within the full scope of the claims.

To be enabling, the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re*

Wright, 27 USPQ2d 1510 (Fd. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547, the court recited eight factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re*

Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The invention is drawn to the prophylaxis or treatment of diverse gastrointestinal conditions, symptoms, pathologies and characteristics thereof. The relative skill of those in the art is high, generally that of an M.D. or Ph.D. with expertise in the area of gastroenterology.

However, that factor is outweighed by the unpredictable nature of diseases, as irritable bowel syndrome, *inter alia*. The Merck Manual describes the cause of irritable bowel syndrome to be unknown. Further, a perspective of the breadth of gastrointestinal disorders is shown in the table of contents in The Merck Manual. On pages 10-12 of the specification, testimonial Examples 1-3 each describe one of three patients who is suffering from either diarrhea-predominant irritable bowel syndrome or intermittent diarrhea/constipation irritable bowel syndrome.

The present disclosure is clearly not predictable for prophylaxis of any disorder. The disclosure is not commensurate in scope with the instant claims.

The amount of direction or guidance provided and the presence or absence of working examples

There are no working examples drawn to a prophylaxis modality in which a compound of the present invention is shown to be clinically effective for the substantially

unrelated conditions, symptoms, pathologies, or characteristics thereof, that are encompassed in the claim language. No guidance is provided drawn specifically to methods of prophylaxis. Such an assertion is clearly beyond the scope of the instantly claimed invention. The term is an absolute definition that means to stop from occurring and thus requires a higher standard for enablement than does "therapeutic" or "treat". It is well established in the medical arts that the vast majority of diseases suffered by mankind cannot be prevented with current therapies. Within the broadest reasonable interpretation for methods for prophylaxis, the prior art does not recognize methods for predictably preventing recurrences in patients suffering from irritable bowel syndrome.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to doses and dosing regimens drawn to methods for the prophylaxis of any type of IBS that are encompassed in the claim language. The skilled artisan would expect such a therapeutic goal to be very specific and highly unpredictable absent a clear understanding of the therapeutic regimen contemplated for diarrhea-dominant IBS, constipation-dominant IBS and alternating IBS. The instant specification sets forth no such understanding. Absent reasonable *a priori* expectations of success for using balsalazide, or a salt thereof, or a 4-aminosalicylic acid compound modified to include a 4-aminobenzoyl-β-alanine side chain, or a 5-amino salicylic acid compound modified to include a benzoyl- β-alanine side chain, one skilled in the gastroenterology art would have to test extensively various dosages and dosing regimens to discover which is effective. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be

empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

Prophylaxis encompasses the complete and absolute inhibition of the onset of IBS entirely.

Due to the known unpredictability of the art (as discussed *supra*) and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that IBS could be prevented following the administration of balsalazide, or a salt thereof, or a 4-aminosalicylic acid compound modified to include a 4-aminobenzoyl-β-alanine side chain, or a 5-amino salicylic acid compound modified to include a 4-aminobenzoyl- β-alanine side chain. Accordingly, the instant claims do not comply with the enablement requirements of 35 U.S.C. 112, first paragraph, since to practice the claimed invention would require a person of ordinary skill in the art to engage in undue experimentation with no assurance of success.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lin et al., U.S. Patent 6,562,629.

Lin teaches the administration of balsalazide in the treatment of irritable bowel syndrome. See column 18, lines 4-21, where 4- or 5-aminosalicylic acid compounds,

and conjugated derivatives thereof, are taught to be effective antimicrobial and anti-inflammatory agents in methods of treating IBS. See the Abstract. Lin teaches the co-administration of antibiotics in the treatment of IBS, as required by instant claim 10. See Example 3, columns 24-25, and Example 9, columns 29-30, where antibiotics, i.e., neomycin and erythromycin, are, respectively, administered in the treatment of IBS. The open language of the present claims allows for the administration of any number of additional active or inactive agents. According to Lin, useful preparations in IBS therapy include 4-aminosalicylic acid or 5-aminosalicylic acid, such as ipsalazide, sulfasalazine, olsalazine and mesalazine.

Following administration, balsalazide is delivered intact to the colon where it is cleaved by bacterial azoreduction to release equimolar quantities of mesalamine, the therapeutically active portion of the molecule, and 4-aminobenzoyl-β-alanine, an only minimally absorbed and largely inert portion of the molecule.

Therefore, the administration of balsalazide encompasses the limitation of claim 11, i.e., that the 4- or 5-aminosalicylic acid compound is modified to include a 4-aminobenzoyl-β-alanine side chain.

Thus in view of Lin's teaching, one skilled in the gastroenterology art would have been motivated to administer the prodrug balsalazide with a reasonable expectation of treating IBS in a human.

No claim is allowed.

Borody, TJ, U.S. Patent 6,426,338, is cited to show further the state of the art with respect to the administration of 4-aminosalicylic acid derivatives, 5-aminosalicyclic acid derivatives and prodrugs thereof in the treatment of constipation-dominant IBS. See column 1, lines 6-13, and column 2, lines 46-56.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached on 10:30 AM-7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel, may be reached on 591-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

July 1, 2009

/Phyllis G. Spivack/
Primary Examiner, Art Unit 1614